IV. INDUSTRY COSTS

This chapter analyzes the costs to industry associated with EPA regulations of microorganisms under TSCA, as set forth in the rule on microbial products of biotechnology. This chapter is organized into seven sections as follows:

- Section A presents results of the analysis, outlines the approach used to determine industry costs and discusses the limitations of the analysis;
- Section B describes the numbers and types of microorganisms that are reportable under the rule;
- Section C discusses the unit costs of preparing and submitting TSCA Environmental Release Applications (TERAs), Microbial Commercial Activities Notices (MCANs), tiered exemptions and other notifications;
- Section D discusses costs of monitoring and controls that may be required following review;
- Section E discusses other factors that may affect industry costs, such as rule familiarization, user fees, recordkeeping, and costs related to confidential business information (CBI);
- Section F presents examples of possible costs per commercial product; and
- Section G discusses costs of selected alternative regulatory approaches, and presents a sensitivity analysis.

A. Overview of Industry Cost Methodology and Results

This section presents an overview of the methodology used to calculate the quantified costs to industry associated with reporting of microorganism uses under TSCA. In addition, the total and incremental quantified industry costs for Year 1 and Year 5 of regulation are presented.

1. Quantified and Unquantified Costs

The total industry costs of the rule fall into two broad categories -- quantified costs, discussed in this chapter, and non-quantified costs, discussed in both this chapter and Chapter VI on Innovation. The total

quantified costs to industry resulting from the rule on microbial products of biotechnology in 1987 and adjusted values for 1995 are presented in Table IV-1 a and b. As the table indicates, total incremental industry costs for Year 1 range from $894,343 to $2,239,734 in 1987 dollars and between $1,212,729 and $3,037,039 in 1995 dollars. For Year 5, total costs range from $69,696 to $510,722 in 1987 dollars and between $94,508 and $562,539 in 1995 dollars.

These costs reflect only direct, quantified costs of microbial regulation under TSCA. Because there are many costs that could not be quantified, the results should be viewed as a low estimate of costs. The remainder of this section describes the approach used for estimating industry costs.

The total costs to industry provided in this chapter are presented as "Year 1" and "Year 5" costs. Year 1 costs are based on the expected costs for biotechnology products in the early stages of regulation based on limited EPA experience and research in the biotechnology area. Year 5 costs are based on a projection of conditions following industry growth, although even the Year 5 projections may not reflect a "mature" industry, and actual rule impacts may continue to grow for many years.

This analysis uses the current regulatory environment as the baseline for industry costs. Thus, the estimates of total costs resulting from the rule reflect the incremental costs compared to current regulatory practice. Each quantified cost associated with the rule is calculated and then baseline costs associated with current regulatory requirements are subtracted from the totals for each category of costs to determine the total incremental costs attributable to the rulemaking activity.

Table IV-1a. Total Quantified Costs Resulting from Final Rule
(1987 Dollars)

Cost Element	Average Expected Costs	
	Low Cost Case	High Cost Case
Year 1		
Reporting or Submission Costs	$ -34,845	$ 70,390
Post Review Monitoring Costs	$ 142,500	$ 585,000
CBI Substantiation Costs	$ -3,776	$ -5,076
Recordkeeping Costs	$ 4,224	$ 16,940
Rule Familiarization Costs	$ 786,240	$1,572,480
Total Costs to Industry in Year 1	$ 894,343	$2,239,734
Year 5		
Reporting or Submission Costs	$ -66,960	$ -80,402
Post Review Monitoring Costs	$ 142,500	$ 585,000
CBI Substantiation Costs	$ -10,728	$ -13,632
Recordkeeping Costs	$ 4,884	$ 19,756
Rule Familiarization Costs	$ 0	$ 0
Total Quantified Costs to Industry in Year 5	$ 69,696	$ 510,722

Note: Negative costs represent cost savings of the final rule as compared to current policy.

Source: Appendix D.

Table IV-1b. Total Quantified Costs Resulting from Final Rule
(1995 Dollars)

Cost Element	Average Expected Costs	
	Low Cost Case	High Cost Case
Year 1		
Reporting or Submission Costs	$ -47,250	$ 95,449
Post Review Monitoring Costs	$ 193,230	$ 793,260
CBI Substantiation Costs	$ -5,120	$ -6.883
Recordkeeping Costs	$ 5,728	$ 22,971
Rule Familiarization Costs	$1,066,141	$2,132,282
Total Costs to Industry in Year 1	$1,212,729	$3,037,039
Year 5		
Reporting or Submission Costs	$ -90,798	$ -109,025
Post Review Monitoring Costs	$ 193,230	$ 793,260
CBI Substantiation Costs	$ -14,547	$ -18,485
Recordkeeping Costs	$ 6,623	$ 26,789
Rule Familiarization Costs	$ 0	$ 0
Total Quantified Costs to Industry in Year 5	$ 94,507	$ 692,539

Note: The Regulatory Impact Analysis of Regulations on Microbial Products of Biotechnology prepared on January 14, 1994 presented costs in terms of 1987 wage rates. These values have been revised to reflect current wage rates. Specifically, industry costs for selected regulatory options were updated based on estimated increases in labor category cost estimates between March 1987 and June 1995.

According to the Bureau of Labor Statistics Employment Cost index, the average percent rate of increase in total compensation between March 1987 and June 1995 was 35.6% (BLS 1995). This value was used to inflate values for Year 1 and 5 of the quantified industry costs of selected regulatory options in this table.

Negative costs represent cost savings of the final rule as compared to current policy.

Source: Appendix D.

Included in the industry costs are the costs incurred by the 306 universities identified as potentially being involved in biotechnology research covered by TSCA (see Chapter II). It is assumed that the number of universities will not increase from Year 1 to Year 5. Therefore, "Rule Familiarization Costs" for the universities would only apply to Year 1. (Because data were not available to determine how many of the 306 universities identified would actually be involved in TSCA related research for commercial purposes, it is likely that rule familiarization costs attributed to such institutions are overstated).

Certain other industry costs were not quantified with sufficient accuracy to include them in the aggregate cost estimates. These include the reduction in profits that could result if regulation causes delays in product marketing and other costs related to impacts on innovation.

As noted, these other costs are discussed later in this chapter and in Chapter VI on Innovation. Effects on industry costs of higher and lower submission rates are addressed in the sensitivity analysis provided in Appendix D.

2. Limitations of the Analysis

A great deal of uncertainty exists regarding the way in which the rule will impact members of the regulated community. One reason is that while general information requirements are listed in the regulatory text, precise information requirements will depend on future case-by-case Agency decisions. The following sources of uncertainty may affect the estimates of industry costs:

- The nature of risk concerns for future submissions;

- The average depth of information required for submissions, and the nature of monitoring and controls that will be required by the Agency;*
- The extent to which organizations would voluntarily conduct certain activities such as field test monitoring if not required to do so by EPA;
- The number and cost of multiple field test submissions needed during a single research program;
- Uncertainties about industry growth and university activities;
- The number and types of microorganisms that will be exempt from requirements based on Agency regulatory decisions; and
- The likelihood that "new" microorganisms introduced commercially over the next several years will qualify for full or partial exemptions from reporting.

These issues are presented in greater detail in later sections of this chapter.

B. Types and Numbers of Microbial Submissions to EPA

The microorganisms that potentially are reportable under the rule can be classified by the type of microorganism, the application category (e.g., fermentation, agricultural), and the stage of development (research and development (R&D) or general commercial use (GCU)). Different reporting vehicles would be appropriate for these different levels, including the TSCA Experimental Release Application (TERA) and Microbial Commercial Activities Notice (MCAN). Some "new" microorganisms and uses would be eligible for Tier I and II exemptions from reporting for general commercial use and TERA exemptions from reporting for R&D use. Based on the type of microorganism and the stage of development, and the parameters laid out in the rule, different

* Although the information requirements for reporting as set forth in the rule are quite explicit, the way in which EPA interprets the requirements and the amount of data that they will consider to be sufficient will vary on a case-by-case basis.

reporting formats would be appropriate. Table IV-2 presents a schedule of these reporting alternatives as outlined in the rule.

Based on the types of research being conducted currently, the number of submissions in each activity category were estimated for Year 1 (the year following the rule) and Year 5. Table IV-3 shows the number of submissions expected in Year 1 (assumed to be 1994 for this analysis) and Year 5 (assumed to be 1998) under the rule. The estimates are based on the ICF Survey of Biotechnology Companies (ICF 1988 -- see Appendix A) and more recent research performed in October, 1991 (Appendix B). The estimated number of submissions in the table account for Tier I and Tier II exemptions under TSCA §5(h)(4), as well as TERA and MCAN submissions.

Estimates of the expected numbers of submissions may be conservative for the following reasons:

- The assumed industry growth rate of 4 percent is very conservative for a fledgling industry. Some of the biotechnology markets covered by TSCA may experience periods of dramatically higher growth before the industry matures. Also, growth of university testing is not reflected except for releases which are part of a corporate product development program;
- Some reagents may be sold for non-research TSCA applications such as detection of pollutants or food contaminants. The associated microorganisms may be reportable, but were not included in the estimates of submissions.

Nevertheless, the projections presented in Table IV-3 exceed the frequencies of biotechnology premanufacture notifications submitted in recent years. This is believed to be related principally to the optimistic forecasts provided in the survey data cited above, the age of the data, and the continued uncertainty regarding regulatory matters. In addition, the Agency's conservative assumptions regarding academic institutions potentially engaged in TSCA-related research for commercial purposes likely resulted in an

Table IV-2. Schedule of Reporting/Exemption Alternatives

	Default Alternative[a]	Environmental Application Areas Likely Alternative	Closed System (Fermentation) Application Areas Likely Alternative
Lab Research	MCAN	5(h)(3) Exemption or Deferral[b]	5(h)(3) Exemption or Deferral[b]
Field Test	MCAN	TERA Exempt, TERA, or TERA modification	Not Applicable
Test Marketing	MCAN	TME	TME
General Commercial Use	MCAN	MCAN[c]	MCAN, Tier I or II Exemption[c]

Note: Although submission of TERA exempt certifications and TME notices are possible for certain R&D and commercial biotechnology applications, costs have not been attributed to these types of submissions. For purposes of the economic analysis presented here, all costs associated with R&D and commercial application submissions are based on use of the TERA, TERA follow-on, MCAN, TIER I, and TIER II notices. However, this assumption may tend to overestimate costs.

[a] For all new microorganisms, reporting via the MCAN is required unless the submitter qualifies for a reporting exemption and chooses an alternate reporting format. A MCAN may be submitted in lieu of any other reporting format, however.

[b] Under TSCA §5(h)(3), research conducted within a contained structure is exempt from MCAN reporting, as specified in the rule. Additionally, research activities subject to other federal agency jurisdiction can be deferred to the requirements of that agency to avoid duplicate oversight. Recordkeeping requirements may be necessary at the research level for microorganisms subject to TSCA jurisdiction.

[c] Microorganisms at the general commercial use stage of development require the submission of an MCAN, unless they specifically qualify as low risk, in which case a Tier I (one-time certification) or Tier II (fewer reporting requirements and expedited review) Exemption is sufficient. Tiered exemptions are based on provisions of TSCA §5(h)(4).

Table IV-3. Projected Number of Submissions: Final Rule

	Projected Submissions Year 1 (1993)	Year 5 (1997)	Assumed Annual Growth
TERAs	6	6	1%
Follow-on TERAs	18	18	1%
MCAN	4	6	10%
Tier II Exemptions	9	12	10%
Tier I Exemptions[a]	9	12	10%

[a] Because subsequent uses of the same recipient microorganism at the same facility does not require additional certification, the number of actual submissions may be fewer.

Source: Appendix C, Tables C-2 through C-4.

overestimate of the number of TERA submissions attributable to such institutions.

The method of estimating the numbers of microorganisms is described in detail in Appendix C. Uncertainties concerning the estimates of submissions are addressed in the sensitivity analysis presented in Appendix D.

C. Unit Costs of MCANs, Tier I and II Exemptions, and TERAs

Institutions will be required to provide certain information to EPA on the R&D and general commercial uses of "new" microorganisms, by using a TERA, MCAN, or other type of submission. This section describes the method of estimating average submission costs (see Section D of this chapter for a discussion of post-review monitoring and controls costs).

1. Overall Approach to Estimating Unit Costs

Table IV-4 compares average unit costs of various submissions, based on Tables D-3 through D-6 in Appendix D. It is important to note that although average unit costs of submissions are expected to fall within the ranges presented in Table IV-4, individual submissions with especially high or low novelty or risk concerns may have costs outside those ranges.

A major reason for uncertainty concerning unit costs is that the average depth of information needed for each data element listed in the rule depends on the future mix of submissions and on scientific risk concerns, both of which are difficult to predict. It is also important to note that the same unit costs are used for both Year 1 and Year 5.

Although it is possible that increased regulatory experience may lead to lower reporting costs over time, greater novelty and information needs for microorganisms submitted in later years may offset the cost savings. Since it was not possible to predict which of these forces would dominate, this analysis assumes reporting costs do not change over time.

Table IV-4 Average Cost of Preparing a MCAN, Tier I and II Exemptions

Cost Components	MCAN [CFR Reference 725.155, 725.160]	Tier I Exemption [CFR Reference 725.424]	Tier II Exemption [CFR Reference 725.428]
Description of microorganism including verification of taxonomy	Description of morphological and physiological traits of microorganism; verification of taxonomy; phenotypic and ecological characteristics of parental strains and microorganism (2i,ii,4)	Certification of compliance with requirements regarding recipient microorganism and introduced genetic material	Microorganism identity information including type of modification and function of introduced DNA.
Information about microorganism and parental strains behavior on the environment	Description of traits selected for and developed; modification process (3)		Type of modification; function of introduced DNA.
Manufacturing process information, including worker exposure and volume	Information on equipment used to minimize dispersion; procedures for disposal/inactivation; production process; worker exposure; intended manufacturing volume, transport 1(5i,ii,6ii,iii,iv)		Information on equipment used to minimize dispersion; procedures for disposal/inactivation; production process; worker exposure; intended manufacturing volume, transport 1(5i,ii,6ii,iii,iv)
Conditions of activity; human/environmental exposure	Description of intended use of microorganism; summary of health and environmental effects data of parental strains and microorganism (4iv,6vii)		
Information on field release confinement and emergency termination procedures	Information on containment method, engineering controls, and emergency containment procedures (6ii.6v)	Certification of compliance; site of waste disposal	Containment guidelines; description of process and containment information
User Fee	$2,500[a]	0	0
Managerial Review and Submission Writeup	Required	Required	Required
Estimated Percent of MCAN Cost[b]	100%	7%	42%
Total Reporting Cost Per Case	$6,931-$32,722	$727-$1,872	$3,198-$13,408
Review Period	90 days	No review[c]	45 days

[a] User fees are $100 for small businesses.

[b] Calculated from midpoints of ranges.

[c] 10 day advance notice.

Source: Final rule, Appendix D.

Table IV-4 (continued). Average Cost of Preparing a TERA and Follow-on TERA Application

Cost Components	TERA [CFR Reference 725.255]	Follow-on TERA [CFR Reference 725.288]	TERA Exemption [CFR Reference 725.424]
Description of microorganism including verification of taxonomy	Description of morphological and physiological traits of microorganism; verification of taxonomy; phenotypic and ecological characteristics of parental strains and microorganism (1,3iii)	Description of morphological and physiological traits of microorganism; verification of taxonomy; phenotypic and ecological characteristics of parental strains and microorganism (1,3iii)	Certification of compliance with requirements regarding recipient microorganism and introduced genetic material
1 Information about microorganism and parental strains behavior on the environment	Description of traits selected for and developed; modification process (1)	Description of traits selected for and developed; modification process (1)	
Manufacturing process information, including worker exposure and volume	Information on equipment used to minimize dispersion; procedures for disposal/inactivation; production process; worker exposure; intended manufacturing volume, transport (1)	Information on equipment used to minimize dispersion; procedures for disposal/inactivation; production process; worker exposure; intended manufacturing volume, transport (1)	
Conditions of activity; human/environmental exposure	Description of intended use of microorganism and significance of the activity; summary of health and environmental effects data of parental strains and microorganism; planned start date and duration of each activity (1,2,3iv)	Description of intended use of microorganism and significance of the activity; summary of health and environmental effects data of parental strains and microorganism; planned start date and duration of each activity (1,2,3iv)	
Information on field release confinement and emergency termination procedures	Information on number of cells released and methods; characteristics of release site, evidence of notification of state authorities (3i,ii,v)	Information on number of cells released and methods; characteristics of release site, evidence of notification of state authorities (3i,ii,v)	Certification of compliance; site of waste disposal
User Fee	$0	$0	$0
Managerial Review and Submission Writeup	Required	Required	Required
Estimated Percent of TERA Cost	100%	33%[a]	4%
Total Reporting Cost Per Case	$5,330-$54,425	$1,777-$18,142	$727-$1,872
Review Period	60 days	less than 60 days	no review

[a] The cost of submitting a follow-on TERA is estimated to be one-third the cost of submitting a TERA because most of the information will have previously been submitted (Zeph 1990).

Source: Final Rule, Appendix D.

Submission costs for each of the reporting formats can be broken down into scientific and non-scientific costs. The steps used in estimating costs resulting from scientific activities are described first, followed by a discussion of the non-scientific costs and timing considerations.

2. Basic Costs of Scientific Information

Case study data from actual PMNs were not used in the Table IV-4 estimates because past microbial PMNs may not be representative of future submissions and because only very limited information was available from submitters. This section describes the methodology used to develop the estimates presented in Table IV-4.

The approach is based on data developed by SRI International estimating the ranges of labor hours needed to develop information on each of a large number of topics listed in EPA's document, "Points to Consider in the Preparation of TSCA Premanufacture Notices for Genetically Engineered Microorganisms" (EPA 1986a). From among the data elements evaluated by SRI, the Agency selected elements corresponding to the data elements listed in the rule for the MCAN and TERA.* The terminology and level of detail used in the "Points to Consider" document differed from that in the draft rule, so that Agency judgment was required to match the data elements evaluated by SRI with data elements listed in the rule. Finally, in 1991, the Agency re-estimated labor estimates for some data elements.

The Agency used the following standard, fully loaded hourly rates (including base salary plus fringe benefits and overhead costs) to compute 1988 dollar costs (Kearney-Centaur 1988):

---

* Many of the same data elements were used to estimate the costs of both MCANs and TERAs. See Appendix D, Tables D-1 and D-2 for a list of SRI data elements selected.

- $25.00/hour for clerical employee
- $42.78/hour for research technician;
- $54.14/hour for junior professional;
- $71.35/hour for senior professional;
- $103.99/hour for research manager;

Applying these rates to the estimated hours resulted in an average "basic cost" of information for each SRI data element selected.

3. Percent of Basic Scientific Costs Incurred by Submitters

Not all of the "basic cost" of a data element would actually be incurred by submitters, for two reasons. First, EPA may seldom require the full depth of information assumed in the SRI estimates, either because the information is not relevant to a particular application or because risk concerns are low. Second, for many data elements, submitters will develop much of the information for their own research purposes or to satisfy regulatory requirements of other U.S. or foreign agencies (e.g., see PMN P90-1071), and the cost of developing this information should not be attributed to regulation solely.

Therefore, EPA assumed that only a percentage of the basic cost of a data element would be incurred by submitters as solely a result of regulation. The percentages used are presented in Tables D-3 through D-10 in Appendix D. It was not feasible for the Agency to assess each data element individually in order to estimate a suitable percentage; instead, estimates of the percentages were made using the following procedure.

- SRI data originally were presented with a probability rating (presented on a quartile basis) that predicts the likelihood of the submitter having the information in-house or readily available as part of normal research. The probability for any particular data element was presented as a range (e.g. 51-75 percent).
- The Agency used the upper bound for each SRI probability range to compute the average percentage of the "basic cost" actually incurred by submitters for TSCA regulatory purposes. For example, if SRI estimated that 51-75 percent of companies already would have a certain item of information, the Agency assumed that on

average, submitters would incur 25 percent of the basic cost of that data element due to TSCA regulation.

- Some of the data elements of the rule include more than one element of SRI data. Because each piece of SRI data is associated with a separate probability, these cases were calculated using the average percentage, weighted by labor cost, of the elements being grouped together.

- In the case of the data elements of the rule for which the Agency made labor estimates in 1991, the Agency also estimated the range in the percentage of submitters that would need to perform that labor. In these cases, the two endpoints of the range were used for the high and low cost calculations as appropriate.

4. Average Scientific Costs for Each Data Element

For each data element, the percentage was multiplied by the basic cost to give an average cost of developing the information for regulatory purposes. For some data elements, this resulted in a zero average scientific cost. In such cases, there would still be non-scientific submission write-up costs.

For some health and environmental effects data, it was assumed that companies would be required to submit only data already available and would not be required to develop new information. This assumption was based on Agency information requirements for conventional chemical PMNs (Rawie 1990). In such cases, the Agency directly estimated the average number of hours required to supply the listed information.

5. Non-Scientific Reporting Costs

The cost of non-scientific activities was estimated separately by the Agency. "User Fees" were taken directly from rule requirements; "Managerial Review and Submission Writeup" costs were estimated. Managerial review was assumed to require 20 hours by a Research Manager and non-scientific write-up costs were calculated by assuming that a Junior Professional would spend 40-100 hours to prepare submissions (ETD 1988).

"Clerical Preparation," clerical time required to prepare the documents, was estimated to be 8-20 hours.

Certain costs that will be incurred by only a fraction of submitters were not quantified, including costs of negotiation of confidentiality claims, travel by company personnel to host EPA inspections of field test sites, and communications with the Agency such as filing bona fide requests to determine whether a microorganism is reportable, or pre-notice consultations with the Agency to determine exact data requirements.*

6. Treatment of Timing Considerations

Reporting-related costs could be incurred well before the year of the submission, as companies plan ahead for regulatory requirements. However, it was not feasible to estimate the time pattern of such costs, so this analysis assumes that all submission-related costs are incurred in the year of the submission, without discounting or compounding.

In addition, EPA may request additional information from the submitter during review. The amount of additional information requested may vary widely from case to case, depending on the thoroughness of the original submission. The costs presented in Table IV-4 are based on the Agency needs for information and not on whether the information would be provided in the initial submission or during the review period.

The following sections describe costs specific to each type of submission that may be used under the rule.

---

* Such communications are voluntary. In-person consultations are expected to be common in early years, but are expected to give way to telephone consultations as industry gains experience with the rule.

7. Costs Associated with a First-Time TSCA Environmental Release Application (TERA)

Under the rule, TERAs may be submitted for new environmental introductions at the R&D stage in lieu of a MCAN. Table IV-4 indicates the types of information that an institution is asked to provide in a TERA. The average cost of providing these types of information is estimated to fall between $5,330 and $54,425 for one submission for the first strain reviewed in a research program. Additional strains covered in the same TERA or later strains in the same research program would have lower costs. Likewise, those strains deemed exempt from TERA requirements, namely Bradyrhizobium japonicum and Rhizobium meliloti, will have lower costs attributable to the preparation of brief certifications proposed to be required for TERA exempt microorganisms.

The information for a TERA is similar to the information that would be required for a MCAN if the MCAN were submitted for the same small-scale field test. TERA information requirements listed in the rule are generally similar to those listed for a MCAN (with a few differences shown in Table IV-4). However, EPA's risk concerns will be more limited for a given field experiment than for the unrestricted use usually associated with inventory listing. As a result, there will be few differences between TERAs and MCANs in information required for a given field trial. Features other than information requirements may make the TERA more attractive to researchers conducted a field trial than a MCAN (summarized in Appendix C). The Agency expects the TERA approach to be faster and more flexible than the MCAN and the associated TSCA section 5(e) Consent Order (generally attached to a MCAN for a field

trial), such that it would be unlikely for a submitter to file a MCAN instead of a TERA for an R&D field test.*

There also are costs that may result from submission of a TERA or a MCAN for environmental release that are not included in Table IV-4. The cost of monitoring and controls that may be required under a TERA or under a Consent Order for a MCAN are quantified later in this chapter and included in aggregate costs. Costs resulting from withdrawals (or rejections) of submissions, and impacts on innovation are excluded from the aggregate industry costs, but are discussed in Chapter VI. A more detailed description of all of the cost elements and the actual costing analysis are provided in Appendix D, Tables D-3 and D-4.

Under the rule, no reporting would be necessary for research involving microorganisms in contained structures. It is believed that the containment criteria set out in the rule embody current laboratory practice, such that no "upgrading" of lab equipment or procedures to meet the EPA standards would be required.

8. Follow-on and Related TERA Submissions

In the course of a research program, a TERA submitter may elect to make changes in the microorganism, test location, or test protocol. Some of these changes can be made without further reporting, but other changes would require EPA approval or even a new TERA, depending on the wording of the TERA and TERA Agreement, and on EPA's risk concerns.

The amount and cost of any such "follow-on" reporting is difficult to predict. In many cases, follow-on TERAs may require very little new information, so that each could result in very low additional cost for

---

* The impact of delays on profits are discussed in Chapter VI on Innovation.

submitters, but in other cases the cost could be significant. For example, if there is significant uncertainty about the fate of the microorganism in the environment, a follow-on submission might require detailed information on a new site of application or on a new monitoring protocol.

The cost analysis provided in this chapter assumes that for each field test for which a TERA is submitted, there will be three follow-on TERAs in the product development process. The costs associated with these follow-on TERAs are assumed to be approximately one third of the cost of the original TERA, or between $1,777 and $18,142 per follow-on TERA (see Appendix D). The costs of minor TERA changes are not quantified in this analysis.

In certain cases, microorganisms may be exempt from full R&D reporting under TSCA §§ 725.238 and 725.239. Specifically, R&D activities involving environmental testing of well-characterized microorganisms, (Bradyrhizobium japonicum and Rhizobium meliloti), are exempt from TERA reporting. The exemption requirements restrict the inclusion of structural genes encoding marker sequences to those that have been previously reviewed by EPA for use in microorganisms. Additionally, test sites are limited to ten acres per site.

TERA exemption requirements would be limited to the filing of a brief one-time certification identifying the recipient microorganism, introduced genetic material, and a description of containment measures. No prior Agency review would be required; however the exemption certification submitted to EPA should include evidence of notification of state and/or local authorities concerning the planned test, if such notification is required. Costs associated with TERA exemptions are not discussed in the RIA because it was not possible to estimate the proportion of expected submissions that would be eligible for the exemption.

9. Microbial Commercial Activities Notices (MCANs)

An institution currently must submit a Premanufacture Notice (PMN) prior to manufacturing or importing a new microorganism for general commercial use. Under the rule, MCANs would be submitted for commercial-level uses of "new" microorganisms, if they do not qualify for a reporting exemption. A MCAN also could be submitted in lieu of a TERA for an R&D activity involving environmental introduction.

Table IV-4 lists the general categories of information that an institution must provide to the Agency in a MCAN and shows the estimated average cost of preparing a MCAN. This cost falls between $6,931 and $32,722. This range is based on the following assumptions: 1) the low cost is estimated to be the cost associated with a MCAN preceded by a TERA (i.e., some costs would have been incurred during the TERA process, and hence, would not be incurred for the MCAN), and 2) the high cost is estimated to be the cost associated with a closed system MCAN (i.e., a released MCAN is preceded by a TERA and therefore has a lower cost than a closed system MCAN that is never preceded by any type of submission).

In the case that a company decides to submit a TME for a closed system application, it is expected that the company would eventually need to submit a MCAN. Because the MCAN would require all the information that was submitted in a TME and this analysis accounts for the costs of collecting the information required for a MCAN, the cost of potential TME submissions is assumed to be accounted for in the submission costs for a MCAN.*

* In reality, TME costs would be incurred first and the following MCAN would be assumed to have minimal costs. The analysis presented here includes all costs for TMEs in MCAN costs.

10. Tiered Exemption Applications

In some cases, "new" microorganisms may be exempt from full reporting under TSCA Section 5(h)(4). Tier I and Tier II reporting exemptions are possible under §5(h)(4). The reporting requirements and a comparison of the individual data elements for each type of application notification are presented in Table IV-4.

To apply for a Tier I exemption, companies would file a brief one-time certification identifying the recipient microorganism and certifying that the company meets specified criteria for the recipient microorganism, introduced genetic material, and containment. No prior Agency review would be involved.

Previous analyses related to the impact of New Chemicals Program submissions (e.g., low volume exemptions and polymer exemptions) have estimated the costs for certifications to consist of a certain amount of time for legal or senior managerial review of the information included in the certification (EPA-ETD 1982). The length of the required review would be proportional to the amount of information that is included in the certification plus the amount of other information that must be certified (e.g., use of correct procedures).

The burden associated with the Tier I exemption can be estimated in a similar manner. These exemptions will require some amount of research manager or attorney labor to review the points that are being certified for content and accuracy. Although it may be reasonable for some organizations to generate records or documentation that support their certification, this information would be readily available if the proper procedures were in place so that there would not be any significant burden associated with compiling the information. The certification for a Tier I exemption would include the following pieces of information, and is valid for subsequent uses of the same

recipient microorganism at the same facility (so long as other Tier I exemption conditions are met):

- name and address of manufacturer or importer;
- certification of the following:
  - that the recipient microorganism is listed in §725.420;
  - compliance with the requirements for introduced genetic material as described in §725.421;
  - compliance with the containment requirements described in §725.422 and §725.424(a)(3);
- site of waste disposal and the type of permits for disposal, the permit numbers and institutions issuing the permits; and
- certification statement as required under §725.25(b).

The information that must be reviewed for this certification is equivalent to the majority (90 percent by labor cost) of the data elements of a MCAN. Assuming that review time is proportional to the time required for submission of data, the labor required for the certification is about 7 to 18 hours of Research Manager time.* This labor time translates to a cost of about $727 to $1,872 per Tier I exemption.

For the Tier II exemption, limited information about the microorganism and its containment would be required. The exact reporting requirements for the Tier II exemption are compared to the requirements for the MCAN in Table IV-4. The industry cost for a Tier II exemption was estimated by comparing its data requirements to data requirements for a MCAN. The scientific data elements required for a Tier II exemption, similar to a Tier I exemption, have 100 percent probability that the information would already be readily

---

* The labor estimates for the submission of MCANs and TERAs include 8 to 20 hours for a research manager to review the contents of the submission. However this estimate may be conservative considering the fact that microorganisms listed under 720.420 do not require evaluation.

available. Thus, only costs, such as managerial review time and submission preparation contribute to the estimated cost for a Tier II exemption. Based on these assumptions, the estimated cost of the Tier II exemption is between $3,198 and $13,408 (see Appendix D).

D. Post Review Monitoring, Reporting, and Controls

EPA has statutory authority under Section 5(e) of TSCA to prohibit or limit production of a substance following review of a notification for a commercial product. Under this authority, the Agency may impose a variety of restrictions. For example, in the case of microorganisms, submitters may be required to provide additional data on the use or toxicity of a microorganism and its products, limit an environmental application to certain locations, monitor the microorganism, or implement controls to reduce unintentional releases from a closed facility or dispersal from a field test site. Under the rule, TERA submitters would be bound to follow monitoring and confinement procedures described in the TERA or TERA Agreement.

It is difficult to predict the extent to which monitoring and controls may be required in the future, since this could depend on the future mix of submissions and the nature of Agency risk concerns. However, based on experience with microbial PMNs submitted to date and on Agency judgment, the following assumptions were used in this analysis:

- Some field experiments will have monitoring requirements attributable to EPA. Using the estimate that between 0 and 25 percent of monitoring costs are attributable to EPA (see below), this analysis applies the midpoint of 12.5 percent to all cases.*

* The analysis presented in this RIA assumes that all field tests require monitoring and that monitoring costs are the same for each TERA. In actuality, some TERAs will incur lower costs of monitoring or no costs at all, while other TERAs will incur fewer monitoring costs. Monitoring costs in the current analysis are distributed evenly across all TERAs because of uncertainties regarding the nature of expected submissions.

- No general commercial uses will have monitoring requirements attributable to EPA regulation because it is unlikely that microorganisms will be allowed into general commercial use unless risk concerns have been allayed (e.g., through monitoring at the R&D level). Minor costs related to labeling or restrictions on method of application were not quantified.*

- §5(e) Consent Orders are rarely needed for microorganisms intended for general commercial use in closed system applications. This is based on Agency's experience to date, that some small proportion of submissions -- probably less than 10 percent -- could result in §5(e) Consent Orders imposing containment requirements. Data were not available to estimate costs of any such consent orders.

Monitoring due to a Consent Order or TERA Agreement could vary widely from case to case. Furthermore, in some cases a submitter may plan to conduct certain monitoring and control activities even if not required to do so by the Agency, so that some requirements might actually add little extra cost. For these reasons, it is difficult to accurately predict the average costs of post review monitoring and controls due to regulation. For purposes of this analysis, costs of monitoring and controls for released microorganisms were estimated based on information gathered from industry and university researchers that are familiar with the field test practices and the impacts of other regulations on these practices (see Appendix B). Agency experts were also consulted.

Industry and university researchers indicated that the initial monitoring costs for an environmental application ranged from $100,000 to $600,000, but that in subsequent tests the costs dropped dramatically to between $30,000 and $60,000. They also agreed that while regulations could account for a significant portion of these costs, many of the monitoring practices were

---

* Carol Rawie of the Regulatory Impacts Branch, Economics and Technology Division, Office of Toxic Substances, U.S. Environmental Protection Agency has prepared two memoranda, dated August 15 and August 16, 1990, respectively that outline data collected through conversations with the following EPA staff: Elizabeth Anderson, Michelle Bree, Ronald Evans, Gerald LaVeck, Larry Zeph, and Mark Segal.

necessary parts of the scientific method used for the tests. On average, these researchers estimated regulation to account for between 20 and 25 percent of the total monitoring costs (see Appendix B).

While it was assumed that the experience of these sources was representative of some subset of all potentially regulated research activity in environmental application areas, Agency experts noted that monitoring requirements could be much less stringent in many cases, and in some instances monitoring conducted solely to satisfy regulatory concerns may not be required at all (as demonstrated in the recent case of field tests of Rhizobium meliloti strain conducted under TSCA). Therefore to reflect the potential for this variability in regulatory monitoring requirements, a range of 0 to 25 percent was used in estimation calculations. Thus, this analysis assumes that 12.5 percent of total monitoring costs are attributable to the rule and calculates the average monitoring costs imposed by the rule to be between $12,500 and $75,000 for a "first-time" TERA and between $3,750 and $7,500 for a "follow-on" TERA.

E. Other Costs

In addition to submission and monitoring/control costs, there are a number of cost factors that contribute to the overall costs of regulations to the biotechnology industry. These costs are discussed in the remainder of this section and can be categorized as follows:

- Costs of rule familiarization;
- Recordkeeping;
- Confidentiality claims; and
- Delays, product withdrawals, and product rejections.

1. Costs of Final Rule Familiarization

This section discusses the costs that each institution may incur in becoming familiar with the rule. Some rule familiarization costs can be attributed to specific submissions and so are included in the submission cost analysis. However, before any submissions are made, an organization may bear a one-time cost of learning about the regulations affecting microorganisms and, in some cases, about the Toxic Substances Control Act.

The one-time rule familiarization costs are calculated by multiplying the expected unit cost of reviewing and learning about the rule by the number of companies that were identified as working with microorganisms in market areas subject to TSCA. As identified in the ICF Survey of Biotechnology Companies, there were 72 such companies and 306 universities either working in TSCA microbial market areas at the time of the survey, or planning to do so by 1993 (ICF 1988 -- see Appendix A). For this analysis, it was assumed that all institutions potentially affected by the rule would become familiar with microbial regulation under TSCA, including those working only with naturally occurring microorganisms, in Year 1, and that only those additional organizations that entered the TSCA biotechnology market between Year 4 and Year 5 would incur rule familiarization costs in Year 5.*

The estimated average cost of rule familiarization per institution is between $2,080 and $4,160, based on the assumption that an average of 20 to 40 hours of time from an attorney or other senior professional at $103.99/hour

* This may somewhat overstate the number of companies becoming familiar with the rule in Year 1, and understate the number in Year 5, since some companies may delay rule familiarization until they are close to field testing or commercialization. Further, many institutions may not perform TSCA-related work for commercial purposes; thus, the level of effort expended to fully understand the entire rule would not be necessary.

would be required to become familiar with requirements for microbial submissions under TSCA. This average cost is based on Agency judgment and is consistent with an estimate of rule familiarization costs made by a trade association (ABTA 1989).

Total rule familiarization costs for Year 1 are estimated to be between $786,240 and $1,572,480. The number of companies expected in Year 5 is calculated by multiplying the number of companies in Year 1 by the industry growth rate of 4 percent per year for the five year period 1992 to 1996 and subtracting the number of companies expected in Year 4 from that total. Rule familiarization costs for Year 5 for three new companies are expected to be between $6,240 and $12,480. No new universities were estimated to enter the biotechnology field in Year 5. The new companies would need to familiarize themselves with the current regulatory environment even if a rule were not implemented, so there are no incremental rule familiarization costs in Year 5.

2. Recordkeeping Costs for R&D within a Contained Structure

Under the rule, commercial facilities, research laboratories, and other groups that perform R&D experiments within a contained structure on certain classes of microorganisms ultimately intended for applications not specifically exempted by TSCA will be eligible for a "contained structure" exemption under §5(h)(3) of TSCA. While a similar exemption is available under current policy, under the rule researchers will be required to maintain additional records which support their eligibility for the exemption. Academic as well as commercial facilities working with microorganisms at the R&D level in contained structures may need to keep records depending on the type of microorganism under investigation and the expected commercial nature of the product.

The National Institutes of Health (NIH) biosafety level containment requirements and the way these requirements were implemented by the NIH Office of Safety were used as a model to estimate the activities and associated costs for containment that will be required as a result of the rule. This system was used because most academic and industrial institutions currently comply with the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH 1986). The NIH Guidelines describe four levels of containment, from the least stringent (level 1, also called BL1) to most stringent (level 4, or BL4). The level of containment for a particular microorganism is determined by evaluating the characteristics of that microorganism. More stringent or higher containment in general correlates with higher levels of hazard, either human or environmental. Because the focus of biomedical research is on human pathogens, a strong focus on the procedure for ensuring appropriate containment in the NIH system is protection of human health. Microbial products in TSCA market areas, however, are likely to present fewer human health hazards than the human pathogens.

EPA recordkeeping requirements would require that institutions working with eligible microorganisms select containment in light of current information and practice regarding exposure, release, and inactivation. The recordkeeping requirements involve preparation of a brief written statement, or, if the institution uses a specific form, that form. The types of information to be maintained for recordkeeping would include an identification of the microorganism, a description of the containment and inactivation measures selected, and a brief statement on why these measures were selected. The controls selected could be indicated by reference to existing standard, such as the containment levels described in the National Institutes of Health "Guidelines for Research Involving Recombinant DNA Molecules."

Because the NIH guidelines and the procedures of the NIH Office of Safety are used as models, this RIA also estimates the costs associated with a biosafety officer verifying that the laboratory in question meets the BL2 or BL3 containment conditions.*

In order to estimate the burden to individual facilities associated with the recordkeeping requirements, it is necessary to (1) determine the number of subject facilities; (2) establish the number of laboratories utilizing microorganisms that are potentially subject to the rule; and (3) estimate the costs of recordkeeping both for selecting and describing the appropriate containment conditions, and verifying for BL2 or BL3 labs that the selected containment conditions were employed. The remainder of this section addresses the burden to users associated with recordkeeping for these contained structure R&D uses.

a. Number of Subject Institutions

All commercial facilities, research laboratories, and other groups that perform contained R&D on certain classes of microorganisms ultimately intended for applications or releases covered by TSCA could potentially be required to perform recordkeeping regarding the conditions of containment. In addition to 72 private companies working on biotechnology products for use in markets subject to TSCA (ICF 1988), ICF estimates that there are approximately 306 university research facilities involved in microbial research potentially subject to TSCA. This estimate is based on the assumption that an indicator of the number of colleges and universities performing biotechnology research related to markets covered by TSCA is equal

* This analysis assumes BL2 and BL3 containment requirements for some TSCA laboratories. rDNA microorganisms could necessitate more stringent containment conditions than BL1, while microorganisms requiring BL4 containment most likely would not be used for TSCA applications.

to the number (306) of universities receiving grants from NIH for rDNA research (NIH 1988). However, because the universities receive government funding and are required to follow NIH guidelines for recordkeeping, their recordkeeping costs would not be attributable to the rule. Thus, only 72 private companies were considered to be potentially subject to the recordkeeping requirements under TSCA, (ICF estimates). For the rule, however, fewer than 72 institutions will be subject to these requirements because only 26 percent of the experiments conducted by these organizations deal with "new" microorganisms subject to TSCA (ICF 1988).

Also, based on the NIH Office of Safety Model estimates of the number of facilities at these 72 companies conducting research related to TSCA market areas that have containment levels of BL2 or higher are required. EPA estimates (OPTS 1991) that approximately 5 percent of TSCA biotechnology research would require containment levels higher than BL1. Finally, it is assumed that the number of facilities per institution where TSCA-related research is being done ranges from 1 to 3 (OPTS 1991).

b. Number of Microorganisms per Institution

Each facility or institution involved in experimentation with subject microorganisms in contained facilities will be required to keep records on each distinct microorganism that is being investigated. It is estimated that 5 to 10 distinct microorganisms are being studied at each commercial or university establishment. The estimated recordkeeping costs do not reflect the fact that many of these 5 to 10 microorganisms could be variants of the same microorganism under study at a facility. These variants would all be used under very similar containment conditions and could be treated as a single recordkeeping group. In light of this fact, the estimate of 5 to 10 distinct microorganisms studied by an institution would be used

under similar containment conditions represents an assumption that may tend to overstate the costs of the required recordkeeping (OTS 1991, ICF estimates).*

c. Unit Cost of Recordkeeping per Microorganism

The unit cost of recordkeeping was estimated by contacting safety officials at local institutions that are already keeping and reviewing similar records and by EPA estimates. These sources have estimated that between 15 and 30 minutes of a researcher's time would be required to assemble these records. Another 15 to 30 minutes of a research manager's time would be required to certify a microorganism record (OPTS 1991). Hence, the unit costs of these "per microorganism" records range from $44 to $88, using the labor category costs for senior scientist and research manager.

In addition, over the period of time the microorganism is studied, verification of use of selected containment procedures may be necessary in 5 percent of the labs performing research covered by the rule. EPA assumed, based on contacts with safety officials, that this verification of containment equipment and procedures will require between 30 and 60 minutes of a biosafety officer's time per year per facility (OPTS 1991). For purposes of estimating the total costs of this portion of the recordkeeping requirements, the number of separate verification inspections per institution is assumed to be between 1 and 3. Assuming the labor cost of a biosafety officer is equivalent to that of a research technician, the unit costs of these per facility containment verification requirements range from $22 to $44.

---

* It is estimated that experimentation with between 5 and 10 distinct microorganism strains will be manipulated per facility because it is unlikely that, on average, a viable product could be obtained with fewer experiments (OPP 1991, ICF estimates).

d. Total Costs of Recordkeeping Requirements

Projected industry costs associated with the recordkeeping requirements for R&D performed in contained structures for each of the identified options are presented in this section. To determine the costs to industry associated with the recordkeeping requirements, the unit costs for assembling, reviewing, and certifying records were multiplied by the total number of microorganisms for which records must be kept and the number of institutions developing microorganisms subject to the rule. Similarly, the unit costs per facility of the verification provisions of the rule are multiplied by the number of facilities for which it will occur. The total estimated costs associated with recordkeeping attributed to TSCA under the rule are between $4,224 and $16,940 in Year 1 and between $4,884 and $19,756 in Year 5. Tables IV-5 and IV-6 present the estimates for recordkeeping for the regulatory alternatives in which it would be included for Year 1 and Year 5.

While these estimates assume all companies to incur the full costs of the recordkeeping requirements called for in the rule, it is likely that a fair number of facilities may be using the NIH Guidelines in connection with research performed in a contained structure. To the extent that the Guidelines are used (voluntarily or for other reasons), recordkeeping costs are overstated.

3. Confidential Business Information (CBI)

In some cases, companies must provide an explanation for claiming certain information in a TERA, MCAN, Tier I Certification or Tier II exemption to be TSCA Confidential Business Information (CBI), and may need to negotiate with the Agency to resolve disputes concerning these claims. These costs are discussed quantitatively in Appendix E. The unit cost associated with CBI

substantiation for a first-time TERA is estimated to be between $1,015 and $1,509. For follow-on TERAs it is assumed that some of the information may be able to be reused and the cost for these submissions is estimated to be between $560 and $641. Additional information is required for substantiation of CBI for MCANs and Tier II exemptions, but as with follow-on TERAs some information may be reused if these submissions were preceded by a TERA. The estimated range in CBI substantiation costs for these submissions is from $1,104 and $2,852. This range uses the same assumptions as the range for MCAN reporting costs presented above.

The rule requires all substantiation to be "up front" for all submissions at the general commercial use stage. However a requirement for CBI substantiation for a TERA only in the event of a Freedom of Information Act (FOIA) request has been incorporated into the rule. This approach was an alternative discussed in the proposal. Because it is not possible to predict the percentage of TERAs for which these FOIA requests would be received, this analysis assumes that substantiation will be required for all submissions. However, it is important to note that recent submissions for field research have contained no CBI.

The estimated range in total CBI substantiation costs is from $30,522 to $57,668 in Year 1 and from $36,042 to $71,928 in Year 5.

4. Delays, Product Withdrawal, Product Rejection

For any product subject to notification, industry may bear costs associated with postponement in the development or commercialization of a product due to both the normal regulatory review period and any delays in concluding reviews. For example, while reviews of past PMNs for most contained microorganisms at general commercial use have been completed during the 90-day statutory review period, reviews of voluntary PMNs for field tests

Table IV-5. Year 1 Costs of Recordkeeping Associated with Contained Experiments under TSCA

Alternative[a]	Number of Institutions Subject to Regulatory Option	Percent of Experiments Working with New Microorganisms	Number of Facilities Subject to Verification[b]		Number of Records Generated[c]		Unit Cost of Containment Verification		Unit Cost of Recordkeeping		Total Cost of Recordkeeping Requirements	
			Low	High	Low	High	Low	High	Low	High	Low	High
Final Rule	72	26	4	11	94	187	$22	$44	$44	$88	$4,224	$16,940
Alternative 1	72	26	4	11	94	187	$22	$44	$44	$88	$4,224	$16,940
Alternative 2	72	100	4	11	360	720	$22	$44	$44	$88	$15,928	$63,844
Alternative 3	72	100	4	11	360	720	$22	$44	$44	$88	$15.928	$63.844

[a] Alternatives are outlined in Table IV-7.

[b] The number of facilities subject to verification is equal to: 72 companies * 0.05 at BL2 or higher = 3.6 companies. 3.6 companies * 1 to verifications per company = 4 to 11 verifications for the industry for each option.

[c] The number of records generated is equal to: 72 companies * 5 to 10 records per company = 360 to 720 records. Multiplying this figure by the percent of experiments subject to oversight generates the number of records for each option.

Sources: ICF 1987, NIH 1989, OTS 1991.

Table IV-6. Year 5 Costs of Recordkeeping Associated with Contained Experiments under TSCA

Alternative[a]	Number of Institutions Subject to Regulatory Option	Percent of Experiments Working with New Microorganisms	Number of Facilities Subject to Verification[b]		Number of Records Generated[c]		Unit Cost of Containment Verification		Unit Cost of Recordkeeping		Total Cost of Recordkeeping	
			Low	High	Low	High	Low	High	Low	High	Low	High
Final Rule	84	26	4	13	109	218	$22	$44	$44	$88	$4,884	$19,756
Alternative 1	84	26	4	13	109	218	$22	$44	$44	$88	$4,884	$19,756
Alternative 2	84	100	4	13	420	840	$22	$44	$44	$88	$18,568	$74,492
Alternative 3	84	100	4	13	420	840	$22	$44	$44	$88	$18,568	$74,492

[a] Alternatives are outlined in Table IV-7.

[b] The number of facilities subject to verification is equal to: 84 companies * 0.05 at BL2 or higher = 4.2 companies. 4.2 companies * 1 to 3 verifications per company = 4 to 13 verifications for the industry for each option.

[c] The number of records generated is equal to: 84 companies * 5 to 10 records per company = 420 to 840 records. Multiplying this figure by the percent of experiments subject to oversight generates the number of records for each option.

Sources: ICF 1987, NIH 1989, OTS 1991.

have frequently required more than 90 days to complete. These delays, however, may decline as industry gains experience with microbial regulation under TSCA. In addition, although the target TERA review period stated in the rule is 60 days, this too may affect companies' marketing and commercialization plans.

These review periods could create additional costs for submitters or could affect R&D strategies. It was not feasible to quantify the impacts as part of aggregate industry costs, but these costs are discussed in detail in Chapter VI on Innovation as well as in Appendix F.

Similarly, withdrawal of a microbial submission as a result of regulatory review may result in foregone profits or foregone product benefits. These effects are also discussed in Chapter VI.

F. Per Product Costs of Reporting and Controls

Per product costs associated with reporting and controls vary according to the nature of the microorganism, its application, and the number of submissions required before a product can be commercialized.* Appendix F contains information on product costs that are derived by changing various assumptions regarding commercialization and product development.

G. Costs of Regulatory Alternatives and Sensitivity Analysis

This section presents estimated industry costs of selected regulatory options. It also examines the sensitivity of quantified industry costs to variations in certain assumptions and estimated values.

---

* Per-product costs may vary depending on the type of product and/or the regulatory approach. It is important to investigate this issue because the impacts on a per-product basis depend on per-product costs.

1. Regulatory Alternatives

In seeking an optimal framework within which to conduct regulatory oversight of microorganisms under TSCA, the Agency examined a number of alternative approaches both to defining the universe of affected microorganisms and to fashioning an efficient screening strategy. The alternatives, the salient differences between which can be seen from examining Table IV-7, generally comprise a spectrum of oversight in terms of the overall volume of microorganisms screened. The various alternatives also present options with respect to the level of scrutiny afforded certain individual submissions, as presented in Table IV-8.

Beginning at the leftmost column in the table (Current Regulatory Environment), the regulated microorganisms are defined as intergeneric or "new" microorganisms. The first three alternatives, including implementing current policy via rulemaking, the rule and Alternative 1, subject the fewest microorganisms to EPA oversight, relative to the remaining alternatives which appear to their right on the chart. These two remaining alternatives, Alternatives 2 and 3, include intrageneric, engineered, and naturally occurring microorganisms in the regulatory framework. Though eliminated from further consideration (for reasons described below), Alternatives 2 and 3 are presented here to illustrate the effects on administrative proposals of changes in the number of submissions. The rationale for selecting the rule is set forth below.

2. Evaluation of Regulatory Alternatives

Tables IV-9 and IV-10 present total quantified costs for regulatory options in Year 1 and Year 5. The costs presented in the tables indicate that the cost of additional reporting for more extensive regulatory coverage may be high, particularly in the case of a more mature industry. For example,

Alternative 1 resembles the rule, but provides for no §5(h)4 exemptions at the general commercial use stage, or in connection with the TERA. This alternative would increase benefits by reducing risks associated with uncertainty in what EPA believes to be categories of microorganisms which are likely to have some, but perhaps not significant, potential to exhibit new traits.

However, while society would benefit marginally from a reduction in these risks, regulatory costs associated with such benefits were judged to be inordinately high. As Table IV-10 indicates, total costs could increase, relative to rule costs, by a factor of 3 at the low end of the estimated cost range developed for Alternative 1 in Year 5, with the high end of the range increasing by a factor of 2.5 in Year 5. Thus, this alternative would be expected to increase overall regulatory costs substantially, while providing only marginal benefits.

Alternatives 2 and 3 were rejected on similar grounds. In each case, significant numbers of additional submissions would be required relative to the rule and Alternative 1 (survey results indicate a substantial number of naturally occurring and other "non-new" microorganisms to be in use or under development for applications falling within the jurisdiction of TSCA - see Table A-3, Appendix A) while only marginal benefits could be expected. As noted above, these alternatives will not be considered further; however, they illustrate the dramatic effect of the 5(h)(4) exemptions on regulatory costs when the number of submissions is significantly increased (Alternative 2 incorporates the exemptions, while Alternative 3 does not).

EPA also considered and rejected an alternative which would formalize the current regulatory environment. Under such an approach, the Agency would proceed with rulemaking to implement its 1986 Policy Statement requiring

Table IV-7. Options Matrix for Biotechnology Rulemaking

	Current Regulatory Environment[a]	Final Rule	Alternative 1	Alternative 2	Alternative 3
Type of microorganism subject	Intergeneric microorganisms	Intergeneric microorganisms	Intergeneric microorganisms	All microorganisms (naturally occurring included)	All microorganisms (naturally occurring included)
Deferral to Other Agencies	No formal procedure	Formal Deferral	Formal Deferral	Formal Deferral	Formal Deferral
Microorganisms in Commercial R&D					
Lab Scale	Small Quantities Exemption Provision	Contained Structure Exemption Provision	Contained Structure Exemption Provision	Contained Structure Exemption Provision	Contained Structure Exemption Provision
Environmental Testing	Voluntary Reporting (PMN)	Reporting required (TERA); TERA Exemption Provision	Reporting required (TERA)	Reporting required (TERA); TERA Exemption Provision	Reporting required (TERA)
Microorganisms in General Commercial Use					
Pilot Scale	TME Provision	TME Provision	TME Provision	TME Provision	TME Provision
Commercial Distribution & Use	Reporting required (PMN)	Reporting required (MCAN)	Reporting required (MCAN)	Reporting required (MCAN)	Reporting required (MCAN)
	No exemption provision	Tier I Exemption Provision; Tier II Exemption Provision	No exemption provision	Tier I Exemption Provision; Tier II Exemption Provision	No exemption provision

[a] This RIA uses the current regulatory environment as the baseline for the total cost estimates of the other regulatory alternatives. This case is intended to reflect the cost of implementing the current policy with a rulemaking. The only incremental cost in this case is for rule familiarization.

Table IV-8. Assumptions by Regulatory Alternative

Assumption[a]	Final Rule	Current Framework Rulemaking[b]	Alt. 1	Alt. 2	Alt. 3
Growth Rates					
Industry	4%	4%	4%	4%	4%
New Environmental Applications	1%	1%	1%	-1%	-1%
New Closed System Applications	10%	10%	10%	4%	4%
Years of R&D for New Environmental Applications	5	5	5	2	2
Years of R&D for New Closed System Applications	2	2	2	1	1
Follow-ons per TERA	3		3	1	1
R&D to Commercial Dropout rate	50%	50%	50%	30%	30%
Commercial Submission Distribution					
MCAN	20%	100%	100%	20%	100%
Tier I	40%			40%	
Tier II	40%			40%	
Percentage of facilities requiring recordkeeping for containment verification	5%		5%	5%	5%
Percentage of microorganisms requiring recordkeeping	26%		26%	100%	100%
Percentage of R&D Field Tests requiring monitoring[c]	100%		100%	100%	100%

[a] The changes in these assumptions between alternatives reflect the different expectations for the sectors of the biotechnology market that would be subject to various requirements as the requirements of the rule change. The sensitivity analysis, presented in Appendix D, shows the effect that changing some of these assumptions would have on the estimated costs of the final rule.

[b] In addition to the differences shown in the table, the submission unit cost range used to calculate the cost of this option is different than for the other options to account for the fact that commercial submissions would not be preceded by submissions at the R&D level. Appendix D presents the estimates for the costs of biotechnology PMN submissions that are used.

[c] Not all field tests would require monitoring; without an estimate of the percentage that would require monitoring, however, this analysis assumes a "worst case" scenario.

Sources: Appendix A, Appendix B, and Appendix D.

Table IV-9a. Year 1 Quantified Industry Costs of Selected Regulatory Options (thousands of 1987 dollars)

Option	Reporting	Monitoring	CBI Substantiation	Recordkeeping	Rule Familiarization	Total
Final Rule						
Low	-34.8	142.5	-3.8	4.2	786.2	894.3
High	70.4	585.0	-5.1	16.9	1,572.5	2,239.7
1986 Policy Statement (Mandatory Aspects)	a	a	a	a	786.2	786.2
Low					1,572.5	1,572.5
High						
Alternative 1:						
Low	54.6	142.5	6.2	4.2	786.2	933.7
High	522.8	585.0	20.6	16.9	1,572.5	2,717.8
Alternative 2:						
Low	911.0	1,202.5	204.8	15.9	786.2	3,120.4
High	7,551.4	6,105.0	412.9	63.8	1,572.5	15,705.6
Alternative 3:						
Low	1,646.3	1,202.5	286.5	15.9	786.2	3,937.5
High	11,270.9	6,105.0	652.4	63.8	1,572.5	19,664.7

Table IV-9b. Year 1 Quantified Industry Costs of Selected Regulatory Options (thousands of 1995 dollars)

Option	Reporting	Monitoring	CBI Substantiation	Recordkeeping	Rule Familiarization	**Total**
Final Rule						
Low	-47.19	193.23	-5.15	5.70	1,066.09	1,212.67
High	95.46	793.26	-6.92	22.92	2,132.31	3,037.03
1986 Policy Statement (Mandatory Aspects)	a	a	a	a	1,066.09	1,066.09
Low					2,132.31	2,132.31
High						
Alternative 1:						
Low	74.04	193.23	8.41	5.70	1,066.09	1,266.31
High	708.92	793.26	27.93	22.92	2,132.31	3,685.34
Alternative 2:						
Low	1,235.32	1,630.59	277.71	21.56	1,066.09	4,231.26
High	10,239.70	8,278.38	559.90	86.51	2,132.31	21,296.79
Alternative 3:						
Low	2,232.38	1,630.59	388.49	21.56	1,066.09	5,339.25
High	15,283.34	8,278.38	884.65	86.51	2,132.31	26,665.33

[a] Costs for the current regulatory environment in this analysis are used as the baseline. The only incremental costs involved with implementing these requirements with a rulemaking would be the rule familiarization costs. This analysis assumes that rule familiarization costs are the same for both the current policy and the final rule. While it is likely that actual costs of familiarization for the current policy would be less than those for the final rule, no quantitative approach for reducing the costs was available.

Note: The Regulatory Impact Analysis of Regulations on Microbial Products of Biotechnology prepared on January 14, 1994 presented costs in terms of 1987 wage rates. These values have been revised to reflect current wage rates. Specifically, industry costs for selected regulatory options were updated based on estimated increases in labor category cost estimates between March 1987 and June 1995.

According to the Bureau of Labor Statistics Employment Cost index, the average percent rate of increase in total compensation between March 1987 and June 1995 was 35.6% (BLS 1995). This value was used to inflate values for Year 1 and 5 of the quantified industry costs of selected regulatory options in this table.

Figures may not sum to totals due to rounding.

Source: Appendix D.

Table IV-10a. Yesr 5 Quantified Industry Costs of Selected Regulatory Options (thousands of 1987 dollars)

Option	Reporting	Monitoring	CBI Substantiation	Recordkeeping	Rule Familiarization	Total
Final Rule						
Low	-67.0	142.5	-10.7	4.9	0.0	69,7
High	-80.4	585.0	-13.6	19.8	0.0	510.7
1986 Policy Statement (Mandatory Aspects)						
Low	a	,	.	a	0.0	0.0
High					0,0	0.0
Alternative 1:						
Low	52.3	142,5	2.5	4.9	0.0	202.2
nigh	522.8	585.0	20.6	19.8	0.0	1.148. !
Alternative 2						
Low	974.6	1.170.0	206.8	18.6	0.0	2.370.0
High	7.738,2	5.940.0	431.4	74.5	0.0	14.184. I
Alternative 3:						
Low	2.860.2	1.170.0	313.2	18.6	0.0	4.361.9
High	13.417.1	5.s40.0	725. I	74.5	0.0	20.156.7

Table IV-10b. Year 5 Quantified Industry Costs of Selected Regulatory Options (thousands of 1995 dollars)

Option	Reporting	Monitoring	CBI Substantiation	Recordkeeping	Rule Familiarization	Total
Final Rule						
Low	-90.85	193,23	-14,51	6.64	0 0	94.51
High	-109.02	793.26	.1844	26.85	0.0	692.51
1986Policy Statement (Mandatory Aspects)						
Low	a	a	a	a	0.0	0.0
High					0.0	0.0
Alternative 1:						
Low	70.92	193 .23	3.39	6.64	0.0	274,18
High	708.97.	793.26	27.93	26.85	0.0	1.5%.s2
Alternative2:						
Low	1,321.56	1.3s6 .52	280.42	25.7.7.	0.0	3,213.72
High	10,492,59	8,0s4.64	584.98	101.02	0.0	19,253.64
Alternative3:						
Low	3.m843	1$5.52	424.70	25.22	0.0	5914.74
High	18,193.59	8,0%.64	983.24	101.02	0.0	27.332,49

[a] Costs for the **current regulatory environment in this analysis are used as the baseline.** The only incremental costs involved with implementing these requirements with a rulemaking would be the rule familiarization costs This analysis assumes that rule familiarization costs are the same for both the current policy and the final rule. While it is likely that actual costs of familiarization for the current policy would be less than those for the final rule, no quantitative approach for reducing the costs was available.

Note: The Regulatory Impact Analysis of Regulations on Microbial Products of Biotechnology prepared on January 14, 1994 presented costs in terms of 1987 wage rates. These values have been revised to reflect current wage rates. Specifically, industry costs for selected regulatory options were updated based on estimated increases in labor category cost estimates between March 1987 and June 1995.

According to the Bureau of Labor Statistics Employment Cost index, the average percent rate of increase in total compensation between March 1987 and June 1995 was 35. 6% (BLS 1995) . This value was used to inflate values for Year 1 and 5 of the quantified industry costs of selected regulatory options in this table

Figures may not sum to totals due to rounding.

Source: Appendix D.

premanufacture notification for all microorganisms at the general commercial use stage and requesting voluntary reporting of field tests. While workable and thus far accepted by the regulated community, this alternative would be less efficient and possibly provide fewer absolute risk reduction benefits to society (due to the voluntary nature of the reporting requirements for field testing). [Thus, although the rule is somewhat more costly than a rulemaking based on current policy, due to the capture of costs of TERA reporting and associated monitoring for a greater number of field trials, the added benefits of efficiency and comprehensive coverage of field research were judged to be of greater value to society.]

EPA concludes that in selecting the rule, it has put forward the most efficient scheme of oversight from among the alternatives considered, while at the same time ensuring that the vast majority of microorganisms presenting the greatest uncertainty will be subject to regulation.

A detailed description of the calculations and assumptions that were used to estimate the costs for each of these seven regulatory alternatives is provided in Appendix D, following the sections on development of the unit costs of the various reporting vehicles.

3. Sensitivity Analysis

The cost estimates in this report are based on numerous assumptions, many of which are subject to substantial uncertainty. Therefore, a sensitivity analysis was conducted to measure the extent to which the results would be affected by changes in some of the key assumptions. The sensitivity analysis, presented in Appendix D, helps identify the areas in which more research would have the greatest value in improving the results.